

TRANSLATION

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>C1-A0323P</b>	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. <b>PCT/JP2004/018501</b>	International filing date (day/month/year) <b>10.12.2004</b>	Priority date (day/month/year) <b>12.12.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>C07K16/28, C12N16/00, C12N1/15, C12N1/19, C12N1/21, C12N5/00, C12P21/02, A61K98/395, A61P35/00, A61P35/02, A61P37/02,</b>		
Applicant <b>CHUGAI SEIYAKU KABUSHIKI KAISHA</b>		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>	
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>	

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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International application No.

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Box No. 1	Basis of the report
1.	<p>With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.</p> <p><input type="checkbox"/> This report is based on translations from the original language into the following _____ which is the language of a translation furnished for the purposes of:</p> <p><input type="checkbox"/> international search (Rule 12.3 and 23.1(b))</p> <p><input type="checkbox"/> publication of the international application (Rule 12.4)</p> <p><input type="checkbox"/> international preliminary examination (Rule 55.2 and/or 55.3)</p> <p>2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):</p> <p><input checked="" type="checkbox"/> the international application as originally filed/furnished</p> <p><input type="checkbox"/> the description:</p> <p>pages _____ as originally filed/furnished</p> <p>pages* _____ received by this Authority on _____</p> <p>pages* _____ received by this Authority on _____</p> <p><input type="checkbox"/> the claims:</p> <p>nos. _____ as originally filed/furnished</p> <p>nos.* _____ as amended (together with any statement) under Article 19</p> <p>nos.* _____ received by this Authority on _____</p> <p>nos.* _____ received by this Authority on _____</p> <p><input type="checkbox"/> the drawings:</p> <p>sheets _____ as originally filed/furnished</p> <p>sheets* _____ received by this Authority on _____</p> <p>sheets* _____ received by this Authority on _____</p> <p><input type="checkbox"/> a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.</p> <p>3. <input type="checkbox"/> The amendments have resulted in the cancellation of:</p> <p><input type="checkbox"/> the description, pages _____</p> <p><input type="checkbox"/> the claims, nos. _____</p> <p><input type="checkbox"/> the drawings, sheets/figs _____</p> <p><input type="checkbox"/> the sequence listing (specify): _____</p> <p><input type="checkbox"/> any table(s) related to sequence listing (specify): _____</p> <p>4. <input type="checkbox"/> This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).</p> <p><input type="checkbox"/> the description, pages _____</p> <p><input type="checkbox"/> the claims, nos. _____</p> <p><input type="checkbox"/> the drawings, sheets/figs _____</p> <p><input type="checkbox"/> the sequence listing (specify): _____</p> <p><input type="checkbox"/> any table(s) related to sequence listing (specify): _____</p>

\* If item 4 applies, some or all of those sheets may be marked "superseded."

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International application No.

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
<b>1. Statement</b>			
Novelty (N)	Claims	<u>1-28</u>	YES
	Claims		NO
Inventive step (IS)	Claims	<u>15</u>	YES
	Claims	<u>1-14, 16-28</u>	NO
Industrial applicability (IA)	Claims	<u>1-28</u>	YES
	Claims		NO
<b>2. Citations and explanations (Rule 70.7)</b>			
Documents 1 to 6 below were cited in the international search report:			
Document 1: Sekimoto E. et al., Blood, November 2003, Vol. 102, No. 11, page 933a, Abstract, #3474			
Document 2: Kipriyanov, S.M. et al., J. Mol. Biol., June 2003, Vol. 330, No. 1, pages 99 to 111			
Document 3: Laurent Genestier et al., Blood, 1997, Vol. 90, No. 9, pages 3629 to 3639			
Document 4: Hudson P.J. et al., J. Immunol. Methods, 1999, Vol. 231, No. 1-2, pages 177 to 189. Review			
Document 5: JP 7-503622 A (The Dow Chemical Company), 20 April 1995, entire description			
Document 6: CO M.S. et al., J. Immunol., 1994, Vol. 152, No. 6, pages 2968 to 2976			
Document 1 sets forth a monoclonal antibody (2D7), and indicates that said monoclonal antibody recognizes HLA class I HLA-A.			
Document 2 sets forth a bispecific scFV antibody containing two variable heavy chain domains and two variable light chain domains (see fig. 1, etc.).			
Document 3 sets forth MoAb90 and YTH862, which are			

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

monoclonal antibodies for human HLA class IA.

Documents 4 and 5 both disclose sc(Fv)2.

Document 6 sets forth a method of obtaining DNA which codes monoclonal antibodies.

The invention set forth in claims 1 to 28 involves an inventive step in relation to documents 1 to 6.

The invention set forth in claims 1 to 28 of this application is not disclosed in documents 1 to 6.

The invention set forth in claims 1 to 14 and 16 to 28 does not involve an inventive step in the light of a combination of documents 1, 2 and 6.

It would be easy for a person skilled in the art to use the method set forth in document 6 to obtain the DNA which codes a monoclonal antibody (2D7) set forth in document 1, and to prepare a bispecific scFv antibody of the monoclonal antibody (2D7) using the method for preparing a bispecific scFv set forth in document 2 from the DNA thus obtained.

The invention set forth in claim 1 to 7 and 17 to 28 does not involve an inventive step in the light of a combination of documents 3 to 6. It would be easy for a person skilled in the art to conceive of using the method set forth in document 6 to obtain DNA which codes the monoclonal antibodies MoAb90 and YTH862 set forth in document 3, and to prepare the sc(Fv)2 of the monoclonal antibodies MoAb90 and YTH862 using the methods of preparing sc(Fv)2 set forth in documents 4 and 5 from the DNA thus obtained.

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

The invention set forth in claim 15 involves an inventive step in relation to documents 1 to 6.

The sc(Fv)2 having the amino acid sequence set forth in SEQ ID NO: 2 described in claim 15 is an sc(Fv)2 of a monoclonal antibody (2D7), but said sc(FV)2, as set forth in fig. 4 and 5, has the same activity as 2D7DB which is a diabody of the monoclonal antibody (2D7), and as shown in fig. 6, markedly improves the stability in the blood, and a person skilled in the art would not be able to predict this feature.

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## Supplemental Box Relating to Sequence Listing

## Continuation of Box No. I, Item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
- a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☐ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☒ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
    - ☐ received by this Authority as an amendment\* on \_\_\_\_\_
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

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## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

(IPC) Int.Cl.7

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